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Investigating the most appropriate dose and effectiveness of thiotepa in combination with ifosphamide, etoposide and rituximab in patients with lymphoma arising in the brain or spinal cord

Submission date 03/12/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 03/12/2014	**Overall study status** Completed	
Last Edited 15/02/2023	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-chemotherapy-and-biological-therapy-for-lymphoma-of-the-brain-or-spinal-cord-tier

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-000227-24

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
17668

Study information

Scientific Title
A study of thiotepa, ifosphamide, etoposide and rituximab for the treatment of relapsed or refractory primary central nervous system lymphoma

Acronym
TIER

Study objectives
The phase I dose finding component is a 3+3 cohort design which will recruit up to 18 patients in order to find the MTD of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER). All patients recruited into phase I at the MTD will also contribute towards phase II. The phase II study is based on an A'Hern’s design to assess the activity of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER). 28 patients will be recruited in total in phase II (including some patients from phase I).

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/LO/1568; First MREC approval date

Study design
Non-randomised, interventional

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Primary central nervous system lymphoma

Interventions
Etoposide, 250mg/m2 day 2 of 21 day cycle; Ifosphamide, 2g/m2/day days 2-4 for each 21 day cycle.; Rituximab, 375mg/m2/day days 1-2 for each 21 day cycle; Thiotepa, Chemotherapy (doses 20mg/m2 - 50mg/m2)

Intervention Type
Drug

Phase

Phase I/II

Drug/device/biological/vaccine name(s)
1. Etoposide 2. Ifosphamide 3. Rituximab 4. Thiotepa

Primary outcome(s)
MTD of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER)
Timepoint(s): End of 2 cycles of treatment

Key secondary outcome(s))
1. 2 year event free survival (EFS); Timepoint(s): 2 years after trial treatment
2. 2 year overall survival (OS); Timepoint(s): 2 years after trial treatment
3. 2 year progression free survival (PFS); Timepoint(s): 2 years after trial treatment
4. CR rate after 2 cycles of TIER; Timepoint(s): End of 2 cycles of treatment
5. Overall response rate (Complete Response (CR) + Complete Response: unconfirmed (CRu) + Partial Res; Timepoint(s): end of 2 cycles of treatment
6. Proportion of patients proceeding to high-dose therapy and autologous stem cell transplant (HDT-AS; Timepoint(s): Following trial treatment
7. Rate of successful stem cell harvest; Timepoint(s): After completing trial treatment
8. Toxicity of TIER using the National Cancer Institute Common Terminology Criteria for Adverse Event; Timepoint(s): All cycles of trial treatment

Completion date
31/10/2021

Eligibility

Key inclusion criteria
1 Age ≥ 16 years of age
2. Histologically confirmed* CD20+ Diffuse Large B Cell Lymphoma (DLBCL) confined to the central nervous system
3. Relapsed or refractory primary central nervous system lymphoma (PCNSL) according to the following definition :
3.1. One or two prior chemotherapy regimen(s), of which at least one regimen contained highdose
methotrexate at a dose of >1g/m2.
3.2. Minimum of one cycle containing highdose methotrexate
4. ECOG performance status 0,1 or 2 (or 3 if attributed to lymphoma)
5. Adequate organ function:
5.1. Bone marrow: platelets >80 x109/L, neutrophils >1 x109/L, haemoglobin >80 g/L
5.2. Hepatic: bilirubin <1.5 x upper limit of normal (ULN) (unless isolated unconjugated hyperbilirubinaemia attributable to Gilbert's syndrome)
5.3. Renal: eGFR ≥40ml/min (Cockcroft-Gault)
5.4. Cardiorespiratory (as judged by the Local Investigator): clinically relevant cardiac or pulmonary function tests must be performed if there is a previous history of significant cardiac or pulmonary impairment
6. Able to comply with the scanning requirements of the study
7. Valid Informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
36

Key exclusion criteria
1. Systemic involvement with lymphoma
2. Active infection requiring intravenous antimicrobials
3. Chemotherapy for lymphoma within 4 weeks registration
4. Wholebrain radiotherapy within 6 months of registration
5. Relapse within 1 year of a Thiotepabased autologous stem cell transplant
6. Prior therapy with the RIE (Rituximab – ifosphamide and etoposide) regimen
7. Evidence of HIV or Hepatitis C infection
8. Hepatitis B infection*
9. Serum albumin <25g/l
10. Pregnant and lactating patients (patients of childbearing potential must have a negative pregnancy test prior to study entry)
11. Competent pPatients and competent patients with partners of childbearing potential not willing to use effective contraception during and for 12 months after therapy

Date of first enrolment
12/12/2014

Date of final enrolment
30/04/2019

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Cancer Research UK Clinical Trials Unit
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Study participating centre
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Study participating centre
Aberdeen Royal Infirmary
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Study participating centre
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Study participating centre
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NG5 1PB

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Derriford Hospital
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SM2 5PT

Study participating centre
Royal Hallamshire Hospital
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S10 2JF

Study participating centre
Southampton General Hospital
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SO16 6YD

Study participating centre
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Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name

Leukaemia and Lymphoma Research

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		26/10/2021	15/02/2023	Yes	No
Basic results		15/02/2023	15/02/2023	No	No
HRA research summary			28/06/2023	No	No
Plain English results			25/10/2022	No	Yes